

**GENE-TARGETED ANIMAL MODEL OF APOLIPOPROTEIN E4 DOMAIN  
INTERACTION AND USES THEREOF**

**ABSTRACT OF THE DISCLOSURE**

**[00198]** The invention provides gene-targeted non-human animals comprising a genetically modified apoE gene encodes a recombinant apoE polypeptide displaying domain interaction. The invention further provides cells isolated from the gene-targeted animals, which cells produce a recombinant apoE polypeptide displaying domain interaction. The invention further provides methods of identifying agents that reduce apoE4 domain interaction, and which are useful to treat apoE4-related neurological and cardiovascular disorders.